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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	

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1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,910	DAN ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *5-14,19-21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,15-18 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I (claim 15 and 22, and claim 18 to the extent it reads on soybean) in the reply filed on 30 July 2010 is acknowledged. The traversal is on the ground(s) that each group refers back to linking claim 1; thus similar search terms are needed to conduct the search on all groups. This is not found persuasive because each group requires the searching of different plant species.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-4, 15-18 and 22 are examined. Claims 5-14, 19-21 and 23 are withdrawn from consideration as being drawn to nonelected inventions.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 15-18 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

The term "increasing" in claim 1 is a relative term which renders the claim indefinite. The term "increasing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. "Increasing" relative to what?

Claim 15 is indefinite because in the method of claim 1, what is transformed is a plant cell; in claim 15 a plant cell is not what is transformed.

Claim 15 lacks antecedent basis for the limitation "said plant transformation media containing an effective amount of lipoic acid" in lines 6-7.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Enríquez-Obregón et al (1997, Biotecnologia Aplicada 14:169-174) in view of Packer et al (1995, Free Rad. Biol. Med. 19:227-250). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 November 2009, as applied to claims 1-4. Applicant's arguments filed 5 April 2010 have been fully considered but they are not persuasive.

The claims are drawn to a method of transforming plant cells and regenerating a transformed plant therefrom by culturing the plant cell on media containing the antioxidant lipoic acid.

Enríquez-Obregón et al teach a method for introducing a macromolecule into a sugarcane cell in culture, wherein the method comprises transforming a sugarcane cell with a nucleic acid and culturing the cell on medium comprising an antioxidant at a concentration of 11-750 μM; the presence of the antioxidant increased the explant viability (Table 2; ascorbic acid was used at a concentration of 85 or 170 μM, cysteine at a concentration of 330 or 750 μM, and silver

nitrate at a concentration of 11 or 29 μM). Enríquez-Obregón et al do not teach regenerating a plant from the transformed plant cell or use of lipoic acid as the antioxidant.

Packer et al teach lipoic acid is a biological antioxidant (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using an antioxidant for increasing transformation efficiency taught by Enríquez-Obregón et al, to use lipoic acid as described in Packer et al as the antioxidant. One of ordinary skill in the art would have been motivated to do so because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that Enríquez-Obregón et al provide no teaching regarding the general use of antioxidants and only disclose the use of a very specific antioxidant combination with no indication that any substitute would be beneficial or successful (response pg 7).

This is not found persuasive. Enríquez-Obregón et al teach that three different antioxidants increase explant viability (Table 2) and that one, the only tested for this, increases the percent of gus-positive explants and BASTA resistant calli (Table 3). Enríquez-Obregón et al also state "The inclusion of AO compounds in the culture media decreases the cell death rate in the explants by inhibiting the hypersensitive reactions developed as a response to the damage generated during the manipulation of the tissue (19)." (pg 173, right column, paragraph 3)." This statement and their demonstration of the effectiveness of three different antioxidants provide a teaching regarding the general use of antioxidants. One of skill in the art would expect other antioxidants to have similar effects, especially an antioxidant described as an ideal antioxidant.

Applicant urges that Packer et al discloses the use of lipoic acid in culturing mammalian cells and does not teach any connection for use in plant transformation or culturing; one of skill

in the art would not expect that lipoic acid, disclosed for use in mammalian cell culture, would be a suitable substitutions for an antioxidant in plant cell culture (response pg 8).

This is not found persuasive because Applicant has not explained why one of skill in the art would think that an antioxidant that is rapidly converted to DHLA, that quenches free radicals in lipid and aqueous domains, that acts synergistically with other antioxidants and that chelates metals (pg 228, right column, paragraph 2) would work in mammalian cell culture but not plant cell culture. There is no teaching in Packer et al these properties are specific to mammalian cells. One of skill in the art would expect lipoic acid to scavenge singlet oxygen (pg 229, right column, paragraph 2) and chelate metals (paragraph spanning the columns on pg 230) in media intended for use with plant cells as well as mammalian cells.

Applicant urges that the working examples of the instant specification provide unexpected results, including several fold reductions in browning and number of nontransgenic shoot and several fold increases in number of explants with reduced browning, transgenic events and plants produced, and number of shoots and callus produced (response pg 8-11).

This is not found persuasive because Applicant's comparisons were all to media with no antioxidants. Enríquez-Obregón et al show that the presence of antioxidants increased explant viability by up to 9 fold relative to media without antioxidants (Table 2) and appears to be required for gene transfer in sugarcane (Table 3); the increases are similar to lipoic acid's performance relative to media without antioxidants. To show unexpected results, Applicant should compare media with lipoic acid to media with, for example, ascorbic acid, silver nitrate or cysteine.

Further, objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support. In the instant case, it is not. In Table 4, which shows the effect of various concentration of lipoic acid on shoot regeneration in tomato, results with 10 μM and 50 μM lipoic acid were no different that with the control. In experiments with wheat, 10 μM and 30 μM, showed no difference in transformation efficiency than did the control a and at 100 μM, there was a decrease in transformation efficiency relative to the control (Table 9). In a study of the effect of lipoic acid that different stages of selection and regeneration, one regime, 25-25-50 μM produced the same transformation efficiency as the control (Table 10). In soybean, 10 μM and 50 μM lipoic acids resulted in transformation efficiencies less than the control (Table 12).

Lastly, the claims are directed to use of lipoic acid or its analogs. The specification only shows results with lipoic acid; no results are shown with any of the hundreds of thousands of analogs encompassed by the teachings of pg 6-17 of the specification.

Thus, Applicant has failed to show unexpected results commensurate in scope with the claims.

6. Claims 1-4 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peri et al (1996, Nature Biotechnol. 14:624-628) in view of Packer et al (1995, Free Rad. Biol. Med. 19:227-250). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 November 2009, as applied to claims 1-4. Applicant's arguments filed 5 April 2010 have been fully considered but they are not persuasive.

The claims are drawn to a method of transforming plant cells and regenerating a transformed plant therefrom by culturing the plant cell on media containing the antioxidant lipoic acid.

Peri et al teach in a method of transforming grape cells and regenerating a transformed plant therefrom, culturing the plant cell on media containing the antioxidant polyvinylpolypyrrolidone (PVPP) at a concentration of 25-500 μM increased the number of viable calli and plants obtained and transformation efficiency (Table 1; paragraph spanning the columns on pg 625; Figure 3). The antioxidant was required to obtained stable transformed grape plants (pg 627, left column, paragraph 1-2). Peri et al do not teach use of lipoic acid as the antioxidant.

Packer et al teach lipoic acid is a biological antioxidant (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using an antioxidant for increasing transformation efficiency and making stable transformed grape plants possible taught by Peri et al, to use lipoic acid as described in Packer et al as the antioxidant. One of ordinary skill in the art would have been motivated to do so because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that one of skill in the art would have no expectation of any benefit or success in combining Peri and Packer because out of 11 antioxidant preparations, only one combination showed benefit, thus producing no teaching that antioxidants in general would increase plant viability or transformation efficiency (response pg 12).

This is not found persuasive because a positive effect was seen with PVPP, DTT and PVP/DTT (paragraph spanning the columns on pg 625). One of skill in the art would have been motivated to try lipoic acid Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that neither reference teaches that lipoic acid would be an appropriate substitute for the antioxidant combination of Peri (response pg 12-13).

This is not found persuasive because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that out of 11 antioxidant preparations, only one combination showed benefit, thus teaching away from substituting one antioxidant for another (response pg 13).

This is not found persuasive because out of 12 antioxidant combinations, 3 showed benefit (paragraph spanning the columns on pg 625). Peri et als' showing of the positive effects of a two different antioxidants and Packer et al's teaching that lipoic acid is the ideal antioxidant would have motivated one of skill in the art to try lipoic acid.

Applicant urges that Peri teaches that antioxidants do not increase plant transformation efficiency (response pg 14).

This is not found persuasive because Peri teaches that antioxidants allow regeneration of stable transgenic grape plants (pg 627, column 1, paragraph 2). Peri did not compare the number of transformed cells with and without the antioxidants.

Applicant urges that the working examples demonstrate increased transformation and regeneration efficiency, and a decrease in browning (response pg 14-15).

This is not found persuasive. Applicant's comparisons were all to media with no antioxidants. Peri et al showed that antioxidants increased regeneration efficiency and decreased in browning (paragraph spanning the columns on pg 625); Peri is silent with respect to transformation frequency for cells; production of transformed grape cells was only possible, however, with the sue of antioxidants. To show unexpected results, Applicant should compare media with lipoic acid to media with, for example, PVPP and DTT.

Further, Applicant has failed to show unexpected results commensurate in scope with the claims, as explained above.

7. Claims 1-3 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai et al (US Patent 6,369,298, filed April 1997 in view of Packer et al (1995, Free Rad. Biol. Med. 19:227-250). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 November 2009, as applied to claims 1-3. Applicant's arguments filed 5 April 2010 have been fully considered but they are not persuasive.

The claims are drawn to a method of transforming plant cells and regenerating a transformed plant therefrom by culturing the plant cell on media containing the antioxidant lipoic acid.

Cai et al teach that in a method of transforming sorghum cells and regenerating a transformed plant therefrom, culturing the plant cell on media containing the antioxidant PVPP at a concentration of 250 μM increased transformation frequency (column 23, lines 2-24). Cai et al do not teach use of lipoic acid as the antioxidant.

Packer et al teach lipoic acid is a biological antioxidant (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using an antioxidant for increasing transformation efficiency taught by Cai et al, to use lipoic acid as described in Packer et al as the antioxidant. One of ordinary skill in the art would have been motivated to do so because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that Peri, which Cai cites, shows that use of antioxidants is unpredictable; neither reference suggest use of other antioxidants or use of lipoic acid (response pg 16).

This is not found persuasive because Cai shows that PVPP increased transformation frequency. One of ordinary skill in the art would have been motivated to do so because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2).

Applicant urges that Packer et al discloses the use of lipoic acid in culturing mammalian cells and does not teach any connection for use in plant transformation or culturing; one of skill in the art would not expect that lipoic acid, disclosed for use in mammalian cell culture, would be a suitable substitutions for an antioxidant in plant cell culture (response pg 16-17).

This is not found persuasive because Applicant has not explained why one of skill in the art would think that an antioxidant that is rapidly converted to DHLA, that quenches free radicals in lipid and aqueous domains, that acts synergistically with other antioxidants and that chelates metals (pg 228, right column, paragraph 2) would work in mammalian cell culture but not plant cell culture. There is no teaching in Packer et al these properties are specific to mammalian cells. One of skill in the art would expect lipoic acid to scavenge singlet oxygen (pg 229, right

column, paragraph 2) and chelate metals (paragraph spanning the columns on pg 230) in media intended for use with plant cells as well as mammalian cells.

Applicant urges that the working examples of the instant specification provide unexpected results, including several fold reductions in browning and number of nontransgenic shoot and several fold increases in number of explants with reduced browning, transgenic events and plants produced, and number of shoots and callus produced (response pg 17).

This is not found persuasive Applicant has failed to show unexpected results commensurate in scope with the claims, as explained above.

8. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ciccarone et al (US Patent Application Publication US 2003/0096414, filed March 2001). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 November 2009. Applicant's arguments filed 5 April 2010 have been fully considered but they are not persuasive.

The claims are drawn to a method of transforming plant cells and regenerating a transformed plant therefrom by culturing the plant cell on media containing the antioxidant lipoic acid.

Ciccarone et al teach a method for introducing a macromolecule into a plant cell in culture, wherein the method comprises transforming a plant cell with a nucleic acid and culturing the cell on medium comprising valeric acid (claims 64, 80-82, 92-93). Ciccarone et al teach that an exemplary valeric acid is lipoic acid (¶33, 34). Lipoic acid is preferably used in the concentration range of 0.0004 - 0.01 g/L (Table 1); this corresponds to 1.9 - 48.5 μM. Ciccarone et al do not teach regenerating a plant from the transformed plant cell.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of culturing a transformed plant cell on media containing lipoic acid taught by Ciccarone et al to regenerate the transformed plant cell into a whole plant. One of ordinary skill in the art would have been motivated to do so because the whole plant is the useful product, for example for producing seeds that can be grown in a field.

Applicant urges that neither Ciccarone nor Packer disclose transforming plant cell and regenerating a plant therefrom (response pg 18).

This is not found persuasive because claims 64, 80-82, 92-93 teach a method for introducing a macromolecule into a plant cell in culture, wherein the method comprises transforming a plant cell with a nucleic acid and culturing the cell on medium comprising valeric acid. Packer is not part of this rejection.

Applicant urges that Ciccarone is directed to culturing and transfecting mammalian epithelial cells, and no working examples are produced for plant cells; Packer does not remedy this deficiency (response pg 18-19).

This is not found persuasive because claims 64, 80-82, 92-93 teach a method for introducing a macromolecule into a plant cell in culture, wherein the method comprises transforming a plant cell with a nucleic acid and culturing the cell on medium comprising valeric acid. Packer is not part of this rejection.

Applicant urges that the working examples of the instant specification provide unexpected results, including several fold reductions in browning and number of nontransgenic shoot and several fold increases in number of explants with reduced browning, transgenic events and plants produced, and number of shoots and callus produced (response pg 19).

This is not found persuasive Applicant has failed to show unexpected results commensurate in scope with the claims, as explained above.

9. Claims 1-3, 15-16, 18 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olhoft et al (2001, US Patent Application Publication 2001/0034888) in view of Packer et al (1995, Free Rad. Biol. Med. 19:227-250).

The claims are drawn to a method of transforming soybean cells and regenerating a transformed plant therefrom by culturing the plant cell on media containing the antioxidant lipoic acid.

Olhoft et al teach the antioxidant cysteine at 100 mg/L to 1 g/L (825 μM to 8250 μM) in the co-cultivation and regeneration media, increased transformation frequency in Agrobacterium-mediated transformation of soybean (¶182-213). Olhoft et al do not teach rooting the transformed shoots to produce a transformed soybean plant or use of lipoic acid in the media.

Packer et al teach lipoic acid is a biological antioxidant (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using an antioxidant for increasing transformation efficiency taught by Olhoft et al to use lipoic acid as described in Packer et al as the antioxidant. One of ordinary skill in the art would have been motivated to do so because Packer et al teach that lipoic acid is the ideal antioxidant (pg 228, right column, paragraph 2) and because Olhoft et al suggest that other sulfhydryl-containing agents would be effective to increase transformation frequency in soybean (¶212, 224, 225). It would be obvious to one of ordinary skill in the art to root the resulting transformed shoots, since this would produced transformed plants, which can produce seeds that can be sold.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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October 7, 2010

/Anne R Kubelik/
Primary Examiner, Art Unit 1638